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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/923,243	08/03/2001	Gavin MacBeath	H00498/70162 TJO	9118

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Timothy J. Oyer
c/o Wolf, Greenfield & Sacks, P.C.
Federal Reserve Plaza
600 Atlantic Avenue
Boston, MA 02210-2211

EXAMINER	
CHEU, CHANGHWA J	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 05/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/923,243	MACBEATH ET AL.	
	Examiner	Art Unit	
	Jacob Cheu	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23/17/2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-47 and 105-119* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-47 and 105-119* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

DETAILED ACTION

Applicant's amendment filed on 2/17/2004 has been received and entered into record and considered.

The following information provided in the amendment affects the instant application:

1. Claims 1-27, 48-104 are cancelled.
2. Claims 105-119 are added to the instant application.
3. Currently, claims 28-47, 105-119 are under examination.

Specification Objection

The specification is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (i.e. see page 7, line 9). Applicant is requested to delete all embedded hyperlinks and/or other form of browser-executable codes. See MPEP § 608.01

Claim Rejections - 35 USC § 112

Scope of enablement

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 28-47 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for BSA covalently bind to the chemically derivatized solid support, does not reasonably provide enablement for *any* solid support without pre-treatment. The

specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The instant invention directs to an array comprising at least one type of protein attached to bovine serum albumin (BSA) coated onto a solid support. However, the specification only support that the "coating" notion as recited in claim 28 merely reflects a chemically modified condition, i.e. covalent binding of BSA to the solid support, not any coating, such as non-covalent binding to the solid support. (page 12, line 18-19) Applicant states numerous times in the specification that the solid support has been functionalized, e.g. adding maleimide group to allow for the attachment of protein (page 13, line 18-21), or BSA-NHS slides which have been fabricated with N, N'-disuccinimidyl carbonate for facilitating the attachment of BSA to the glass slides (page 15, line 22-29; page 26, line 8-10), or spotting proteins on the SMA slides which have aldehyde functional groups on the surface (page 26, line 12-16) Additionally, all the results or data have been shown by conducting through the chemically modified slides. (Figure 1-9) Although applicant states that certain embodiments in the instant invention, the linkage of the proteins to the solid support is accomplished through non-covalent interactions, such as van der Walls force, hydrogen bonding, hydrophobic interactions, pi stacking, examples including biotin-streptavidin, metal complex formation, nucleic acid hybridization, antibody-antigen interaction. (page 13, line 26-28) Nevertheless, the above mentioned "non-covalent" are actually used as the linkage between the BSA and the proteins. (page 14, line 10-15) The reason using the chemically modified slides is for the attachment of BSA to the solid support and providing a firm monolayer of BSA for the subsequent linkage of protein for microarray (page 15, line 22-29; page 26, line 8-10; Figure 1-9) No working example or data demonstrates that the BSA is "non-covalently" coated on the solid support. In view of the quantity of experimentation necessary to determine the feasibility of the non-covalent binding of BSA to the solid support in the microarray, the lack of direction or guidance presented, the absence of working examples, the breadth of the claims, and the unpredictability of the results, it would require undue experimentation for one skilled in the art to practice the entire scope of the claimed invention.

3. Claims 105-109 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for BSA, does not reasonably provide enablement for any protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The instant newly added claims direct to an article comprising a solid support, and a polymer immobilized on the said solid support, where the polymer, i.e. *protein*, being configured to become specifically attached to at least one type of chemically unmodified protein. The specification provides guidance, working example and results only on BSA, not any protein. Additionally, applicant states that caseine, glycine, or ethanolamine may act similarly as BSA. (page 4, line 18-19) However, glycine is a not a protein, nonfat milk is a mixture of protein with other molecules, ethanolamine is also not a protein. Because of the unpredictability of protein in its structures and functions, and particularly not *any* protein can behave like BSA, it would impose undue experimentation to one skilled in the art to use the recited invention.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 35, 105-119 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

With respect to claim 35, line 2, "the linkage" lacks antecedent basis.

With respect to claim 105, line 3, "configured" is vague and indefinite. It is unclear what 'configured' applicant refers to.

With respect to claim 115, "chemically unmodified proteins" is vague and confusing. Applicant recites the "chemically unmodified proteins" while subsequently recites this protein attached to the polymer through a "primary amine of the chemically unmodified proteins." Examiner considers that the linkage through such a primary amine on the protein is a "modification". Clarification of the claim language is needed. Similarly, claims 116-119 all share the same problem as claim 115.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

7. Claims 28-33, 35-36, 43-47, 105-113, 115 are rejected under 35 U.S.C. 102(e) as being anticipated by Charych et al. (US 2002/0055125).

Charych et al. teach a protein microarray comprising a solid support coated with BSA and the density spots ranges from about 1 to 5000 spots/ cm^2. (Page 7, Section 0066, and section 0069, line 5-7) The proteins attached to the BSA are naturally folded and functional. (Section 0057, line 17-20) The proteins are "attached" to the BSA through non-covalent binding. (See Figure 4A and 4B) Examiner considers the "*attachment*" of the BSA to the protein is the same illustrated in Figure 4A and 4B where the BSA as the blocking agents to reduce the non-specificity on the solid substrate and attach the neighboring proteins. The proteins are functional, and the solid support can be polymer, glass or metals. (See section 0037) Furthermore,

8. Claims 105-108,110-111, 114, are rejected under 35 U.S.C. 102(b) as being anticipated by Ceriani et al. (US 4572901).

Ceriani et al. teach a method of detecting analytes, i.e. proteins, in a biological sample. Ceriani et al. teach that covalently bound the BSA to the plurality of microplates in order to provide advantages of more stable binding of proteins to the surface, enhancing specific binding and reproducibility. (Col. 7, line 22-28) Ceriani et al. teach using glutaraldehyde as the crossing agents for covalently bound, i.e. Schiff's linkage to the proteins, i.e. antibody to the BSA. (Col. 4, line 48-60)

9. Claims 105-106, 108, 110-111, 114-115, 118 and 119, are rejected under 35 U.S.C. 102(b) as being anticipated by Bosslet et al. (US 5643731)

Bosslet et al. teach a method of using pair of leucine zipper peptides for in vitro diagnosis. Bosslet et al. teach that immobolized a polymer, i.e. protein, on a solid phase where the protein can covalently bound to other ligands, receptors, antibodies. (Col. 4, line 28-35; Figure 1-2) Bosslet et al. teach the covalent linkage can take place through sulfhydryl, amino and maleimido group on the proteins. (Col. 4, line 28-35; Col. 5, line 1-10)

10. Claims 105-110, 115 rejected under 35 U.S.C. 102(e) as being anticipated by Arnold et al. (US 6372425)

Arnold et al. teach coating anibody, i.e. protein, to a solid support selected from dextran, polysaccharide, or silica, and subsequently coating BSA on this matrix. (Col. 17, .ine 10-20; claims 1, 2, 8) The antibody is functional for later detection of analytes.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

13. Claims 28-41, 43-47, 105-119 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ceriani et al. (US 4572901) in view of MacBeath et al. (J. Am. Chem. Soc. 1999 121: 7967-7968).

Ceriani et al. teach a method of detecting analytes, i.e. proteins, in a biological sample. Ceriani et al. teach that covalently bound the BSA to the microplates in order to provide

advantages of more stable binding of proteins to the surface, enhancing specific binding and reproducibility. (Col. 7, line 22-28) Ceriani et al. teach using glutaraldehyde as the crossing agents for covalently bound, i.e. Schiff's and amine linkage to the proteins to the BSA. (Col. 4, line 50-55) Although Ceriani et al. do not explicitly mention other covalent binding mechanisms as recited in the instant claims 37, 39, 40, 116-119, nevertheless Ceriani et al. teach that "the subject composition provide for a strongly *adhering layer* which is highly functionalized to allow for *covalent linking* of a wide variety of materials, such as ligands and receptors." (Col. 7, line 29-33) Therefore, it would have been obvious to one skilled in the art at the time the invention was made to motivate applying Ceriani et al. teaching with other alternative covalent binding such as Michael addition and disulfide bond, with reasonable expectation of success since using other covalent bond linkage is taught or suggested by Ceriani et al. (see above) and it only involves routine practice to replace glutaradehye with other covalent agents to optimize the binding between the BSA and the target proteins.

Furthermore, Ceriani et al. do not teach using a microarry with at least 1000 spots per cm2 for detecting the proteins. MacBeath et al. teach using microarry for mass-screening diagnostic purposes. MacBeath et al. teach a micrarray device with the density of 2000 spots per cm2. (See Figure 4) Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have provided Ceriani et al. with the microarray device as taught by MacBeath et al., since mass-screening by microarray is time and cost saving, one skilled in the art would have adapted MacBeath et al. device to enhance efficiency and reproducibility.

Response to Applicant's Argument

14. Applicant's arguments with respect to claims 28-47 have been considered but are moot in view of the new ground(s) of rejection.

With respect to Charych et al. reference

15. Applicant argues that Charych et al. reference is not a prior art under 102(e) and reserved the right to establish an invention date for the claimed invention that is on or before the effective 35 USC 102(e) date. Examiner had considered applicant's argument with respect to the priority of this case. Thus far, absent of any evidence indicating applicant's superior priority, examiner would still consider this reference as a proper prior art. Furthermore, examiner interprets the recited wording "attached" as "*to connect as adjunct or associated with*". (See Webster's II New Riverside University Dictionary, page 136, 1994) Under this definition, Figures 4A and 4B of Charych et al. reference would read on the instant claim because the BSA is "connect or associate with" the protein, albeit BSA in Charych et al. reference is a blocking agent instead of an adapting agent as recited in the instant invention.

Conclusion

16. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jacob Cheu whose telephone number is 571-282-0814. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jacob Cheu
Examiner
Art Unit 1641

May 12, 2004

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600
05/14/04